Supplemental Information

Table S1. [^{18}F]fallypride Dose Characteristics

	All Scans *n* = 43	Healthy Controls *n* = 22	SCZ *n* = 21	*p*
Dose, mCi	3.02 ± 1.01	3.12 ± .92	2.93 ± 1.10	.54
Injected mass, μg	1.01± 0.19	1.02 ± .16	.99 ± .23	.53
SA, Ci/mmole	1163 ± 542	1190 ± 578	1135 ± 515	.74
fp	.061 ± .019 (*n* = 42)	.065 ± .022	.056 ± .013 (*n* = 20)	.10

mCi, millicurie; μg, microgram; SA, Specific activity; Ci/mmole, curie per millimole; fp, plasma free fraction of [^{18}F]fallypride; SCZ, patients with schizophrenia

Table S2. Prior Studies of Extrastriatal $D_{2/3}$ Receptors in Schizophrenia

Study	*N*, patients / controls	Ligand / modality	Regional findings			
			thalamus	temporal cortex	anterior cingulate	substantia nigra
Suhara *et al.* (1)	11 / 18	[^{11}C]FLB 457 / PET	-	-	↓	-
Tuppurainen *et al.* (2)	7 / 7	[^{123}I]epidepride / SPECT	-	↓	-	-
Talvik *et al.* (3)	9 / 8	[^{11}C]FLB 457 / PET	↓*	-	-	-
Yasuno *et al.* (4)	10 / 19	[^{11}C]FLB 457 / PET	↓	-	-	-
Buchsbaum *et al*. (5)	15 / 15	[^{18}F]fallypride / PET	↓	↓	-	-
Glenthoj *et al*. (6)	25 / 20	[^{123}I]epidepride / SPECT	- **	-	-	-
Kessler *et al*. (7)	11 / 11	[^{18}F]fallypride / PET	↓***	-	-	↑

* lower on R but not in whole thalamus
** R > L in patients
*** lower on L

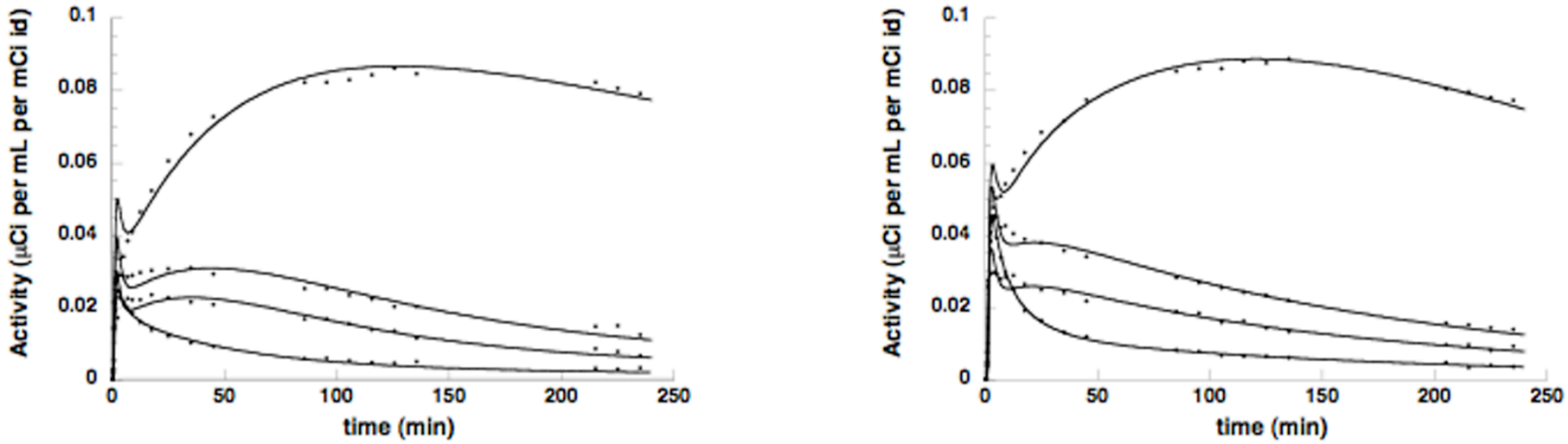

Figure S1. Time activity curves for an individual patient (left) and healthy control subject (right) showing activity for four regions, from bottom of graph: reference region (cerebellum), uncus, thalamus, and post-commissural caudate. Data shown are (filled circles) measured regional decay-corrected but partial volume-uncorrected activity, and (solid lines) 2-tissue compartment model fits to the regional time activity data. See text, "Methods, PET scanning" for description of the sequences of acquisitions and breaks between acquisitions. µCi, microcurie; mL, milliliter; mCi, millicurie; id, injected dose.

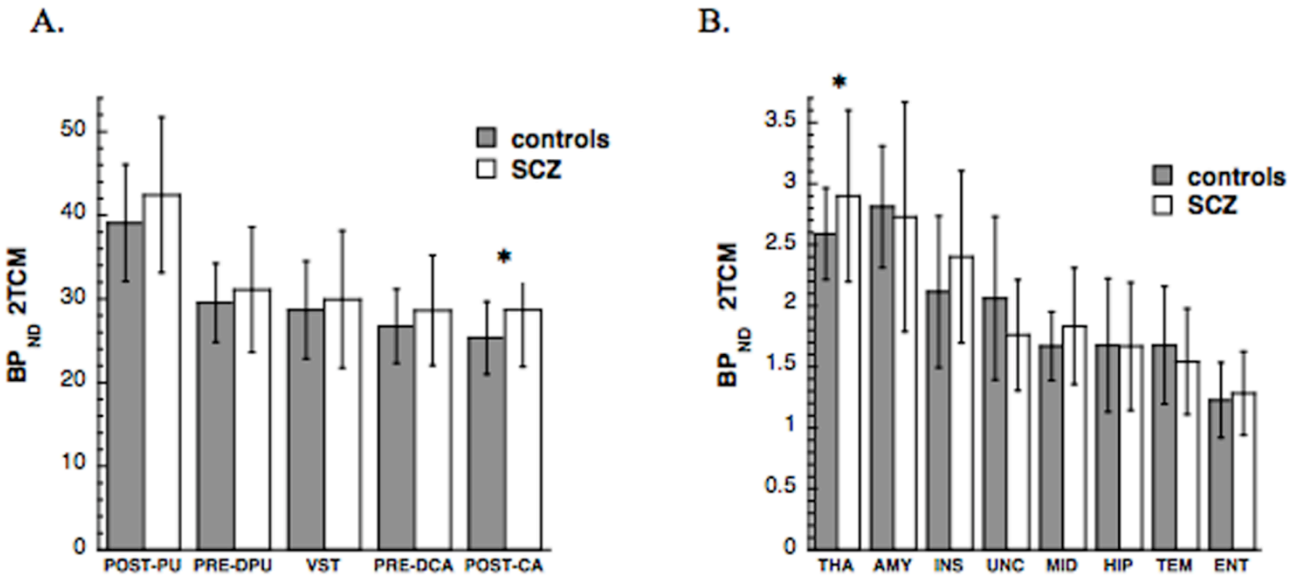

Figure S2. Binding potential relative to nondisplaceable uptake (BP_{ND}, unitless) from the two tissue compartment model (2TCM) in (**A**) striatal and (**B**) extrastriatal regions in patients with schizophrenia (SCZ) and control subjects. (**A**) Striatal subregions: POST-PU = post-commissural putamen, PRE-DPU = pre-commissural dorsal putamen, VST = ventral striatum, PRE-DCA = pre-commissural dorsal caudate, POST-CA = post-commissural caudate. (**B**) Extrastriatal regions: THA = thalamus, AMY = amygdala, INS = insula, UNC = uncus, MID = midbrain, HIP = hippocampus, TEM = temporal cortex, ENT = entorhinal cortex. The y-axis range is an order of magnitude lower in the extrastriatal than the striatal regions. Here and in all 2TCM results the SCZ group includes $n = 20$ subjects with arterial access. Two regions, POST-CA and THA, showed higher binding in SCZ. * Significantly different by analysis of covariance with age as covariate.

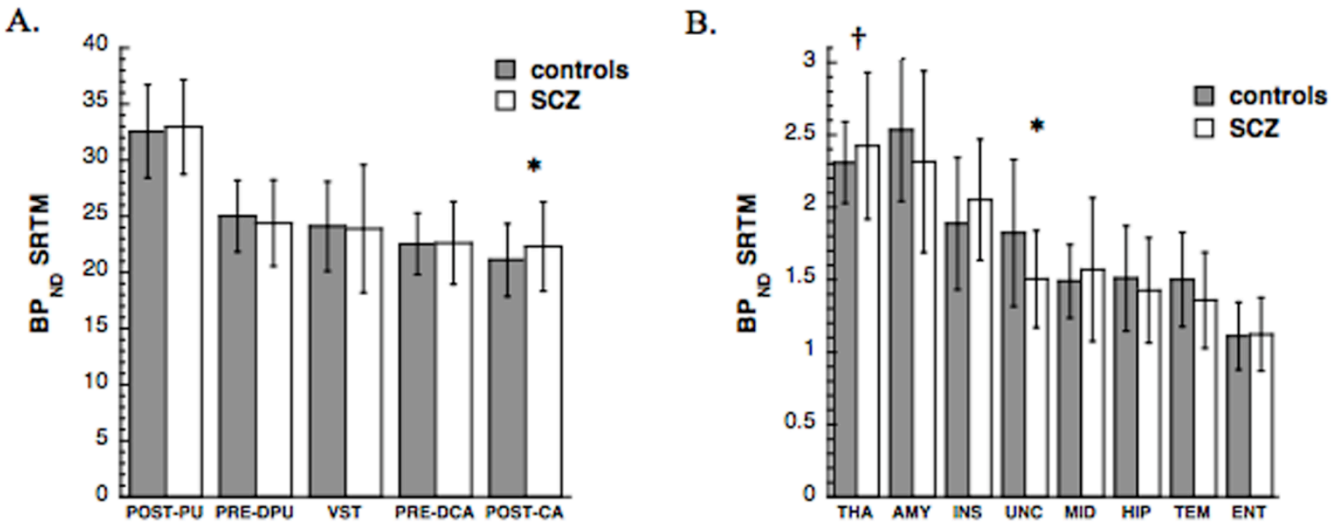

Figure S3. Binding potential relative to nondisplaceable uptake (BP_{ND}, unitless) from the simplified reference tissue model (SRTM) in the same regions shown in Figure S2 in SCZ and control subjects. Here the SCZ group includes all $n = 21$ subjects. The same regions as in 2TCM were elevated significantly (POST-CA) or at trend level (THA) in SCZ, and UNC was lower in SCZ. * Significantly different by analysis of covariance (ANCOVA) with age as covariate. † Different at trend level ($p = .07$) by ANCOVA. Abbreviations as in Figure S2.

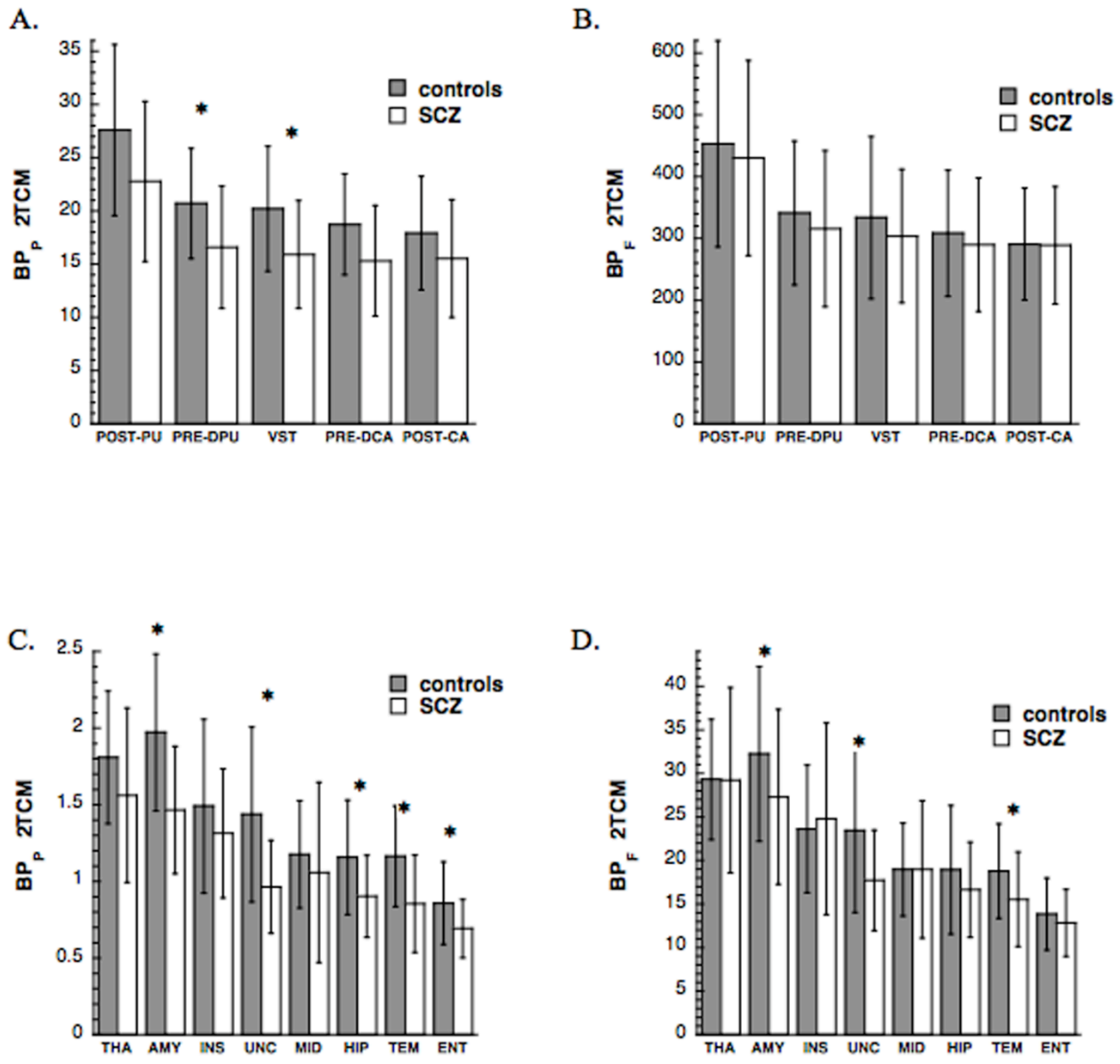

Figure S4. Binding potential relative to total plasma concentration (BP_P, mL/cm^3) shown in left panels (**A** and **C)**, with SCZ significantly lower than controls in multiple regions. Right panels (**B** and **D)** show binding potential relative to plasma free fraction (BP_F, mL/cm^3) for the same regions, which corrects BP_P for plasma free fraction f_P of radioligand, which was lower in the SCZ subjects. After the f_P correction no striatal regions and only 3 extrastriatal regions, including UNC, remained lower in SCZ than controls.
* Significantly different by analysis of covariance with age as covariate. Abbreviations as in Figure S2.

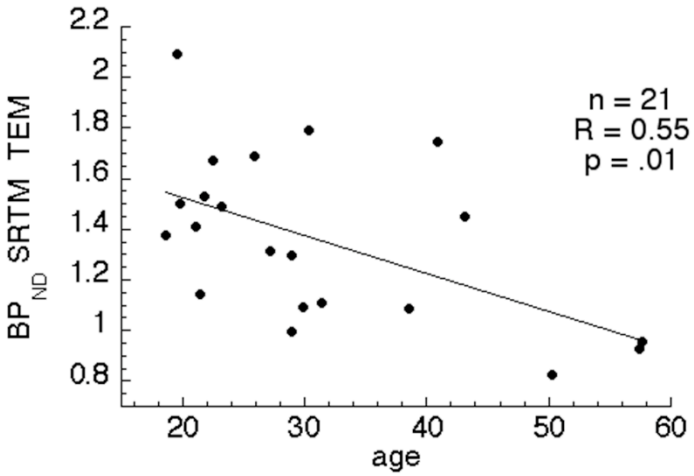

Figure S5. Regression plot of binding potential relative to nondisplaceable uptake (BP_{ND}) from simplified reference tissue model (SRTM) as a function of age showing D_2/D_3 receptor loss with age in patients with schizophrenia in temporal cortex (TEM).

1. Suhara T, Okubo Y, Yasuno F, Sudo Y, Inoue M, Ichimiya T*, et al.* (2002): Decreased dopamine D2 receptor binding in the anterior cingulate cortex in schizophrenia. *Arch Gen Psychiatry* 59:25-30.

2. Tuppurainen H, Kuikka J, Viinamaki H, Husso-Saastamoinen M, Bergstrom K, Tiihonen J (2003): Extrastriatal dopamine D 2/3 receptor density and distribution in drug-naive schizophrenic patients. *Mol Psychiatry* 8:453-455.

3. Talvik M, Nordstrom AL, Olsson H, Halldin C, Farde L (2003): Decreased thalamic D2/D3 receptor binding in drug-naive patients with schizophrenia: a PET study with [11C]FLB 457. *Int J Neuropsychopharmacol* 6:361-370.

4. Yasuno F, Suhara T, Okubo Y, Sudo Y, Inoue M, Ichimiya T*, et al.* (2004): Low dopamine d(2) receptor binding in subregions of the thalamus in schizophrenia. *Am J Psychiatry* 161:1016-1022.

5. Buchsbaum MS, Christian BT, Lehrer DS, Narayanan TK, Shi B, Mantil J*, et al.* (2006): D2/D3 dopamine receptor binding with [F-18]fallypride in thalamus and cortex of patients with schizophrenia. *Schizophr Res* 85:232-244.

6. Glenthoj BY, Mackeprang T, Svarer C, Rasmussen H, Pinborg LH, Friberg L*, et al.* (2006): Frontal dopamine D(2/3) receptor binding in drug-naive first-episode schizophrenic patients correlates with positive psychotic symptoms and gender. *Biol Psychiatry* 60:621-629.

7. Kessler RM, Woodward ND, Riccardi P, Li R, Ansari MS, Anderson S*, et al.* (2009): Dopamine D2 receptor levels in striatum, thalamus, substantia nigra, limbic regions, and cortex in schizophrenic subjects. *Biol Psychiatry* 65:1024-1031.